ChemPubSoc Europe

DOI: 10.1002/ejoc.201900982

EurJOC European Journal of Organic Chemistry

Full Paper

Decarboxylative Alkylation

Copper-Catalyzed Decarboxylative C(sp^2)-C(sp^3) and C(sp)-C(sp^3) Coupling of Substituted Cinnamic Acids and 3-Phenyl Propiolic Acid with N-Tosyl Oxaziridines

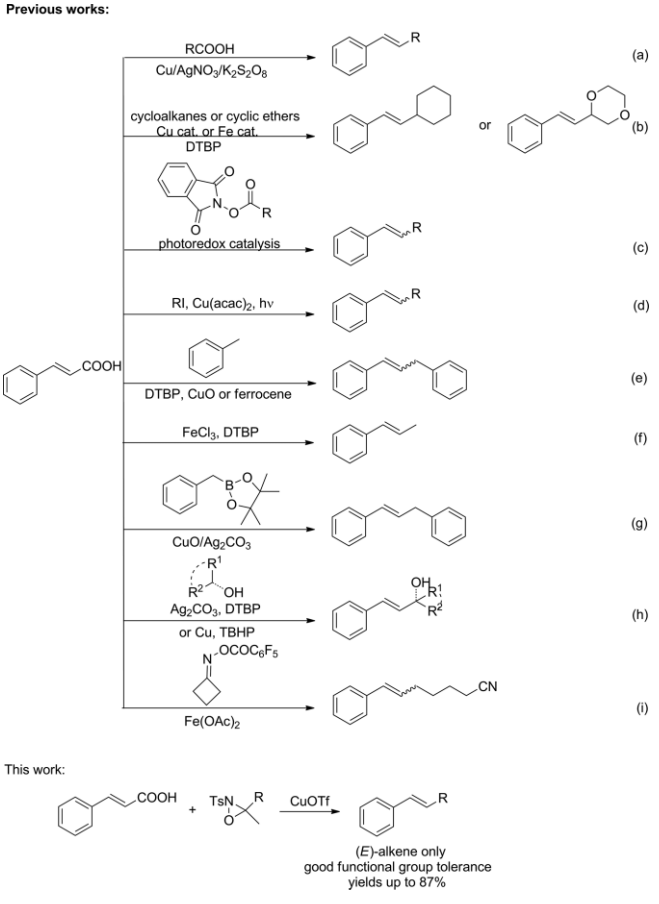
Bich-Ngoc Nguyen*[a] and Hai-Thuong Cao[a]

Abstract: A mild and efficient strategy for decarboxylative C(sp^2)-C(sp^3) and C(sp)-C(sp^3) coupling of α,β-unsaturated carboxylic acids such as substituted cinnamic acids and 3-phenyl propiolic acid with N-Tosyl oxaziridines was developed. The corresponding products were achieved in moderate to good yields with excellent stereoselectivity. Base-free and oxidant-free conditions allow good functional group tolerance. Radical inhibitors such as TEMPO and BHT completely suppressed the reactions suggesting a radical mechanism was involved. This study is supposed to broaden the frontier of oxaziridines' chemistry and to open up a novel cascade for alkylating reagents.

Introduction

Direct transition metal-catalyzed decarboxylative carbon-carbon coupling of carboxylic acids has gained increasing attention of chemists in recent years[1] due to readily available carboxylic acids as starting materials, maximizing atom economy and overcoming the constraint of organometallic reagents. In this field, there is great interest in cinnamic acid as alkenylarenes are widely used in pharmaceuticals, agriculture, and material science.[2] In 2013, Qu[3] introduced copper-silver co-catalysis for the double decarboxylative cross-coupling reaction of cinnamic acids with aliphatic acids (Scheme 1a). However, this protocol only succeeded with secondary and tertiary carboxylic acids. Recently, Pan[4] and Li[5] developed cheaper methods using copper or iron-catalyzed decarboxylative alkylation of cinnamic acids with cycloalkanes and cyclic ethers (Scheme 1b). Mao[6] reported the decarboxylation-methylation of α,β-unsaturated carboxylic acids using $FeCl_3$ (Scheme 1f). Other attempts to construct alkenylbenzenes provided an *E*/*Z* mixture of products[7] (Scheme 1c-e). Meanwhile, a series of decarboxylative C(sp^2)-C(sp^3) coupling reactions of vinylic carboxylic acid were also described by Wu,[8] Liu,[9] Wang[10] and Guo[11] (Scheme 1g–i). Notably, that transition metal-catalyzed decarboxylative carbon-carbon formations, in common, utilize peroxides or other oxidants restricts functional group tolerance. Therefore, the necessity for a mild and stereoselective decarboxylative carbon-carbon coupling of cinnamic acids is still in demand.

Oxaziridines, small organic heterocycles with unusual stability as well as distinctive reactivities, have attracted a lot of interest in the last decades and are potentially universal reagents. Their exposure to chemical or photochemical stimuli leads to various rearrangements to hydroxylamines or nitrones,[12] isomerizations,[13] and eliminations.[14] The role of oxaziridines



Scheme 1. Decarboxylative C(sp^2)-C(sp^3) coupling of cinnamic acids.

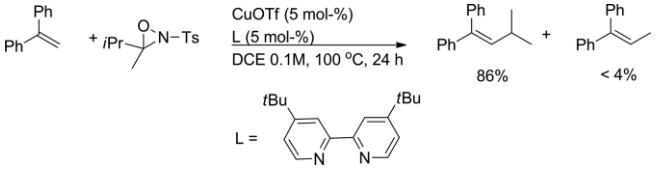
[a] *Department of Physics and Chemical Engineering, Le Quy Don Technical University,*
236 Hoang Quoc Viet Street, Cau Giay District, Hanoi, Vietnam
E-mail: bichngoc.nguyen@lqdtu.edu.vn

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejoc.201900982.

as electrophilic nitrogen source has also been disclosed. There have been a number of aminations of primary and secondary amines to produce hydrazides[15] and hydrazines.[16] Enolates,[17] alkoxides,[18] sulfides[19] and even organometallic species[20] can be aminated in moderate to excellent yields. Nevertheless, the most predominant application of oxaziridines is as electrophilic oxygen atom transfer reagent.[21] Sulfides, with the aid of oxaziridines, can be selectively converted to sulfoxides without or with minor overoxidation to the corresponding sulfones.[22] Moreover, the oxygen atom is successfully transferred to phosphorus,[23] selenium,[24] nitrogen[25] and carbon nucleophiles.[26] In brief, oxidation and amination are the broad ranges of oxaziridine chemistry.

The utility of these intriguing compounds in radical reactions, in contrast, is quite rare. The pioneering research in this field was described by Minisci.[27] Subsequently, Aubé and coworkers reported the first study on intramolecular radical cyclization of oxaziridines.[28] The similar work was published by Black et al.[29] Yoon et al. contributed copper- and iron-catalyzed cycloaddition of N-Sulfonyl oxaziridines with alkenes.[30]

As investigating oxaziridines' reactivities, we found that under copper catalysis, alkyl radicals can efficiently be generated from N-Tosyl oxaziridines (Scheme 2). Inspired by this discovery, we, herein, would like to introduce a decarboxylative alkylation of cinnamic acids using N-Tosyl oxaziridines with high yields and excellent stereoselectivities.



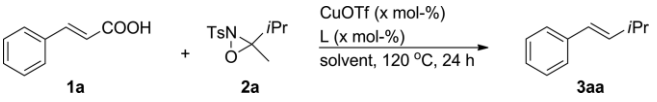
Scheme 2. Alkyl radical generated from the N-tosyl oxaziridine.

Results and Discussion

We initiated our study by heating a benzene solution of *trans*-cinnamic acid **1a** with N-Tosyl oxaziridine **2a** in the presence of a catalytic amount of copper (I) triflate (5 mol-%) and 4,4′-di-*tert*-butyl-2,2′-dipyridyl as a ligand at 120 °C for 24 hours. To our delight, (*E*)-(3-methylbut-1-en-1-yl)benzene **3aa** was obtained in 29 % yield as the sole isomer (Table 1, entry 1). This result encouraged us due to unsymmetrical alkenes are difficult to be achieved in a single step. Then, it was found that with 2 equivalents of cinnamic acid, the yield significantly increased to 58 % (Table 1, entry 3). Changing in the amount of catalyst or temperature did not enhance the result (Table 1, entries 5–7). Surprisingly, in the presence of 1,2-dichloroethane as a combination solvent, **3aa** was furnished in 67 % yield (Table 1, entry 8). The 1:3 (v/v) ratio of benzene and 1,2-dichloroethane respectively was seemed to be the best with 81 % product yield (Table 1, entry 9).

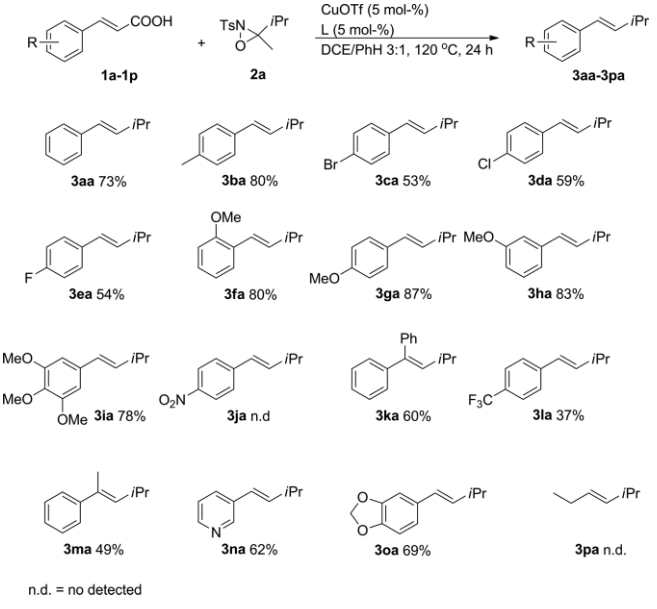
With the optimized conditions in hand, we examined the scope of different substituted cinnamic acids. As shown in Scheme 3, cinnamic acids with the electron-donating group gave excellent yields (**3ba**, **3fa**–**3ia**). Halogen – substituted cinnamic acid also offered desired products in moderate yields (**3ca**–**3ea**). The lower yield was obtained when *p*-trifluoromethyl cinnamic acid was used as the substrate (**3la**) and no reaction occurred with *p*-nitro cinnamic acid. It is important to notice that β-substituted cinnamic acids were also tolerant in our reaction giving products in moderate to good yields (**3ka** and **3ma**). Furthermore, heterocyclic acrylic acid such as *(E)*-3-pyridineacrylic acid afforded the corresponding product **3na** in 62 % yield. Unfortunately, (*E*)-hex-2-enoic acid did not undergo our transformation.

Table 1. Optimization of the reaction conditions.



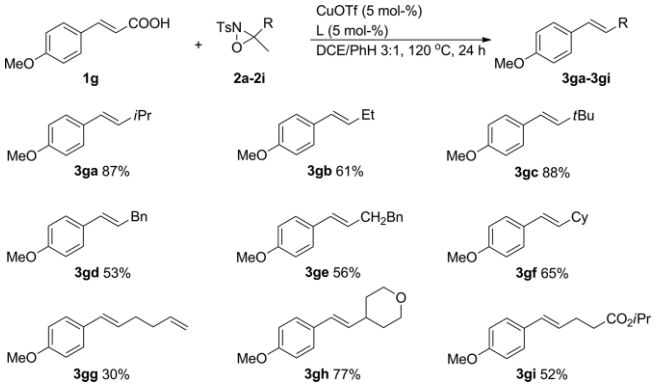
Entry	Acid:Oxaziridine	x	Solvent	Yield[a][%]	
1	1:2	5	PhH	29	
2	1:1	5	PhH	36	
3	2:1	5	PhH	58	
4	3:1	5	PhH	40	
5	2:1	10	PhH	48	
6	2:1	5	PhH	5	at 100 °C
7	2:1	5	PhH	35	at 140 °C
8	2:1	5	PhH/DCE 1:1	67	
9	2:1	5	PhH/DCE 1:3	81(73)	

[a] NMR yield with toluene as the internal standard. The yield in the parantheses is isolated yield.



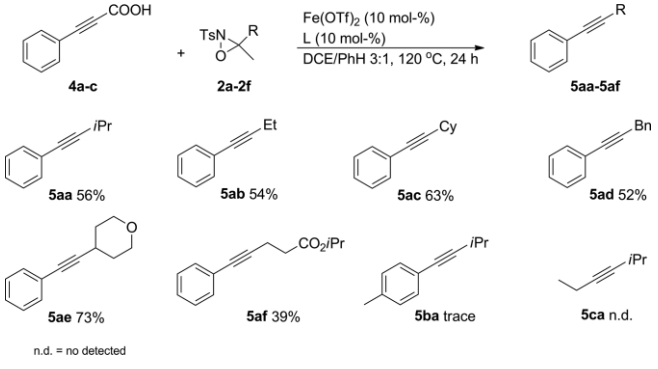
Scheme 3. Scope of cinnamic acids.

Next, various N-Tosyl oxaziridines were investigated with our protocol (Scheme 4). (*E*)-disubstituted ethylenes were successfully installed in moderate to good yields. Interestingly, coupling partner not only included alkyl-, cycloalkyl- but also benzyl-, cyclic ether as well as alkyl moieties bearing other functional groups (**3gi**). Thus, it seemed to provide an efficient synthesis of aryl-substituted allylic esters.



Scheme 4. Scope of oxaziridines.

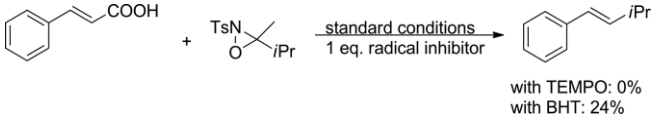
To evaluate the generality of our methodology, we conducted the decarboxylative alkylation of 3-phenyl propiolic acid. After 24 hours, (3-methylbut-1-yn-1-yl)benzene was observed in about 20 % yield. It was hypothesized that the formation of stable (phenylethynyl)copper slowed down the reaction so that $Fe(OTf)_2$ was used instead of copper salt. Undoubtedly, the yield increased up to 56 %. Subsequently, a variety of alkynylbenzenes **5aa–5af** were obtained in moderate yields (Scheme 5). However, 3-(*p*-tolyl)propiolic acid and pent-2-ynoic acid did not undergo our protocol.



Scheme 5. Reactions between 3-phenyl propiolic acid and several oxaziridines.

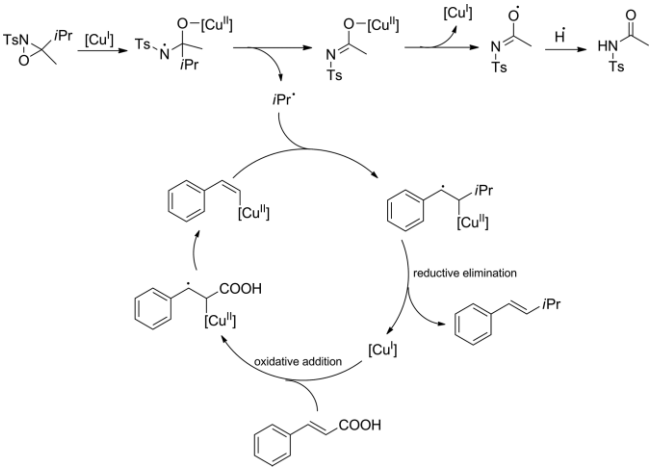
To the best of our knowledge, it is the first example that alkyl aryl acetylenes are directly constructed from the transition metal-catalyzed decarboxylative coupling of aryl alkynyl carboxylic acids without oxidants and bases.

It is noteworthy that radical inhibitors such as TEMPO and BHT completely suppressed our reactions suggesting a radical process was involved (Scheme 6).



Scheme 6. Control experiment.

The detailed mechanism of the alkylation is still under investigation but it is supposed to follow the screenplay described in Scheme 7. Isopropyl radical is generated from N-Tosyl oxaziridines under copper catalysis. Afterward, it is trapped by the intermediate formed between cinnamic acid and the copper salt. The reductive elimination step affords the desired product and reproduces the catalyst itself.



Scheme 7. Proposed mechanism.

Conclusions

In conclusion, we have developed a mild and efficient strategy for stereoselective decarboxylative $C(sp^2)$-$C(sp^3)$ coupling of alkenyl carboxylic acids with N-Tosyl oxaziridines. This protocol also provides an innovative approach for the direct synthesis of alkyl phenyl acetylenes. Moreover, our research is supposed to broaden the frontier of oxaziridines' chemistry and to open up a novel cascade for alkylating reagents. The detailed mechanism of this reaction and other radical reactions of oxaziridines have been investigated in our laboratory.

Experimental Section

A mixture of cinnamic acid **1a** (29.6 mg, 0.2 mmol, 2.0 equiv.), N-Tosyl oxaziridine **2a** (25.5 mg, 0.1 mmol, 1.0 equiv.), $(CuOTf)_2$Toluene complex (1.3 mg, 0.0025 mmol, 5 mol-%) and ligand L (1.3 mg, 0.005 mmol, 5 mol-%) was dissolved in 0.25 mL of benzene and 0.75 mL 1,2-dichloroethane. The reaction mixture was heated in a sealed tube at 120 °C for 24 hours. After cooling to room temperature, 1 mL water was added and the resulting mixture was extracted with dichloromethane. The combined organic extracts were washed with brine, dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with hexane as the eluent affording **3aa** (oil, 10.7 mg, 73 %). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.34 (2H, d, J = 7.7 Hz), 7.29 (2H, d, J = 7.5 Hz), 7.18 (1H, d, J = 7.1 Hz), 6.34 (1H, d, J = 16.0 Hz), 6.19 (1H, dd, J = 16.0 Hz), 2.42–2.50 (1H, m), 1.09 (6H, d, J = 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 138, 137.9, 128.4, 126.8, 126.7, 125.9, 31.5, 22.4. HRMS (ESI-TOF), Calcd. for $C_{11}H_{14}Na$: 169.0988 ($[M + Na]^+$), found 169.0986 ($[M + Na]^+$).

Keywords: C-C coupling · Copper · Decarboxylation · Synthetic methods

[1] a) A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250–11251; b) D. Tanaka, A. G. Myers, *Org. Lett.* **2004**, *6*, 433–436; c)

L. J. Goossen, N. Rodríguez, B. Melzer, C. Linder, G. Deng, L. M. Levy, *J. Am. Chem. Soc.* **2007**, *129*, 4824–4833; d) L. J. Goossen, N. Rodríguez, C. Linder, *J. Am. Chem. Soc.* **2008**, *130*, 15248–15249; e) J. Moon, M. Jeong, H. Nam, J. Ju, J. H. Moon, H. M. Jung, S. Lee, *Org. Lett.* **2008**, *10*-, 945–948; f) H. Kima, P. H. Lee, *Adv. Synth. Catal.* **2009**, *351*, 2827–2832; g) W. W. Zhang, X. G. Zhang, J. H. Li, *J. Org. Chem.* **2010**, *75*, 5259–5264; h) D. Zhao, C. Gao, X. Su, Y. He, J. You, Y. Xue, *Chem. Commun.* **2010**, *46*, 9049–9051; i) L. J. Goossen, B. Zimmermann, T. Knauber, *Beilstein J. Org. Chem.* **2010**, *6*, 43; j) Z. J. Fu, S. J. Huang, W. Su, M. Hong, *Org. Lett.* **2010**, *12*, 4992–4995; k) Z. M. Sun, J. Zhang, P. Zhao, *Org. Lett.* **2010**, *12*, 992–995; l) J. J. Dai, J. H. Liu, D. F. Luo, L. Liu, *Chem. Commun.* **2011**, *47*, 677–679; m) K. Takamatsu, K. Hirano, M. Miura, *Angew. Chem. Int. Ed.* **2017**, *56*, 5353–5357; *Angew. Chem.* **2017**, *129*, 5437; n) X. Tan, Z. Liu, H. Shen, P. Zhang, Z. Zhang, C. Li, *J. Am. Chem. Soc.* **2017**, *139*, 12430–12433.

[2] C. Torborg, M. Beller, *Adv. Synth. Catal.* **2009**, *351*, 3027–3043.

[3] W. P. Mai; G. Song, G. C. Sun, L. R Yang, J. W. Yuan, Y. M. Xiao, P. Mao, L. B. Qu, *RSC Adv.* **2013**, *3*, 19264–19267.

[4] a) J. Zhao, W. Zhou, J. Han, G. L. Y. Pan, *Tetrahedron Lett.* **2013**, *54*, 6507–6510; b) J. Zhao, H. Fang, J. Han, Y. Pan, *Beilstein J. Org. Chem.* **2013**, *9*, 1718–1723.

[5] C. Y. Wang, R. J. Song, W. T. Wei, J. H. Fan, J. H. Li, *Chem. Commun.* **2015**, *51*, 2361–2363.

[6] G. Rong, D. Liu, L. Lu, H. Yan, Y. Zheng, J. Chen, J. Mao, *Tetrahedron* **2014**, *70*, 5033–5037.

[7] a) K. Xu, Z. Tan, H. Zhang, J. Liu, S. Zhang, Z. Wang, *Chem. Commun.* **2017**, *53*, 10719–10722; b) C. Wang, Y. Lei, M. Guo, Q. Shang, H. Liu, Z. Xu, R. Wang, *Org. Lett.* **2017**, *19*, 6412–6415; c) H. Yang, P. Sun, Y. Zhu, H. Yan, L. Lu, X. Qu, T. Li, J. Mao, *Chem. Commun.* **2012**, *48*, 7847–7849; d) H. Yang, H. Yan, P. Sun, Y. Zhu, L. Lu, D. Liu, G. Ronga, J. Mao, *Green Chem.* **2013**, *15*, 976–981.

[8] M. Zhu, Z. Qiu, Y. Zhang, H. Du, J. Li, D. Zou, Y. Wu, Y. Wu, *Tetrahedron Lett.* **2017**, *58*, 2255–2257.

[9] Z. Cui, X. Shang, X. F. Shao, Z. Q. Liu, *Chem. Sci.* **2012**, *3*, 2853–2858.

[10] Z. Fang, C. Wei, J. Lin, Z. Liu, W. Wang, C. Xu, X. Wang, Y. Wang, *Org. Biomol. Chem.* **2017**, *15*, 9974–9978.

[11] J. F. Zhao, X. H. Duan, Y. R. Gu, P. Gao, L. N. Guo, *Org. Lett.* **2018**, *20*, 4614–4617.

[12] T. Połiński, A. Chimiak, *Tetrahedron Lett.* **1974**, *15*, 2453–2456.

[13] a) A. Lattes, E. Oliveros, M. Riviere, C. Belzeck, D. Mostowicz, W. h. Abramskj, C. Piccinni-Leopardi, G. Germain, M. Van Meerssche, *J. Am. Chem. Soc.* **1982**, *104*, 3929–3934; b) J. Aubé, P. M. Burgett, Y. Wang, *Tetrahedron Lett.* **1988**, *29*, 151–154.

[14] a) D. R. Boyd, R. Hamilton, N. T. Thompson, M. E. Stubbs, *Tetrahedron Lett.* **1979**, *20*, 3201–3204; b) W. H. Rastetter, W. R. Wagner, M. A. Findeis, *J. Org. Chem.* **1982**, *47*, 419–422; c) K. Suda, F. Hino, C. Yijima, *J. Org. Chem.* **1986**, *51*, 4232–4239.

[15] a) J. Vidal, J. Drouin, A. Collet, *J. Chem. Soc., Chem. Commun.* **1991**, *0*, 435–437; b) J. Vidal, L. Guy, S. Sterin, A. Collet, *J. Org. Chem.* **1993**, *58*, 4791–4793; c) J. Vidal, J. C. Hannachi, G. Hourdin, J. C. Mulatier, A. Collet, *Tetrahedron Lett.* **1998**, *39*, 8845–8848; d) A. Armstrong, L. H. Jones, J. D. Knight, R. D. Kelsey, *Org. Lett.* **2005**, *7*, 713–716.

[16] N. Richy, M. Ghoraf, J. Vidal, *J. Org. Chem.* **2012**, *77*, 10972–10977.

[17] See ref.[15a].

[18] a) I. C. Choong, J. A. Ellman, *J. Org. Chem.* **1999**, *64*, 6528–6529; b) O. F. Foota, D. W. Knight, *Chem. Commun.* **2000**, *0*, 975–976.

[19] a) A. Armstrong, R. S. Cooke, *Chem. Commun.* **2002**, *0*, 904–905; b) A. Armstrong, R. S. Cooke, S. E. Shanahan, *Org. Biomol. Chem.* **2003**, *1*, 3142–3143; c) A. Armstrong, L. Challinor, R. S. Cooke, J. H. Moir, N. R. Treweeke, *J. Org. Chem.* **2006**, *71*, 4028–4030; d) A. Armstrong, L. Challinor, J. H. Moir, *Angew. Chem. Int. Ed.* **2007**, *46*, 5369–5372; *Angew. Chem.* **2007**, *119*, 5465.

[20] M. Ghoraf, J. Vidal, *Tetrahedron Lett.* **2008**, *49*, 7383–7385.

[21] K. S. Williamson, D. J. Michaelis, T. P. Yoon, *Chem. Rev.* **2014**, *114*, 8016–8036.

[22] a) L. Bohé, M. Lusinchi, X. Lusinchi, *Tetrahedron* **1999**, *55*, 155–166; b) R. D. Mahale, M. R. Rajput, G. C. Maikap, M. K. Gurjar, *Org. Process Res. Dev.* **2010**, *14*, 1264–1268.

[23] A. Arnone, M. Pregnolato, G. Resnati, M. Terreni, *J. Org. Chem.* **1997**, *62*, 6401–6403.

[24] F. A. Davis, J. M. Billmers, O. D. Stringer, *Tetrahedron Lett.* **1983**, *24*, 3191–3194.

[25] F. A. Davis, A. C. Sheppard, *Tetrahedron* **1989**, *45*, 5703–5742.

[26] a) P. Y. Toullec, C. Bonaccorsi, A. Mezzetti, A. Togni, *Proc. Natl. Acad. Sci. U. SA* **2004**, *101*, 5810–5814; b) J. J. Jiang, J. Huang, D. Wang, M. X. Zhao, F. J. Wang, M. Shi, *Tetrahedron: Asymmetry* **2010**, *21*, 794–799; c) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *J. Am. Chem. Soc.* **2006**, *128*, 16488–16489; d) S. Takechi, N. Kumagai, M. Shibasaki, *Tetrahedron Lett.* **2011**, *52*, 2140–2143; e) L. Zou, B. Wang, H. Mu, H. Zhang, Y. Song, J. Qu, *Org. Lett.* **2013**, *15*, 3106–3109.

[27] F. Minisci, R. Galli, V. Malatesta, T. Caronna, *Tetrahedron* **1970**, *26*, 4083–4091.

[28] a) J. Aube, X. Peng, Y. Wang, F. Takusagawa, *J. Am. Chem. Soc.* **1992**, *114*, 5466–5467; b) J. Aubé, B. Gülgeze, X. Peng, *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2461–2464.

[29] D. StC. Black, G. L. Edwards, S. M. Laaman, *Synthesis* **2006**, *12*, 1981–1990.

[30] a) D. J. Michaelis, C. J. Shaffer, T. P. Yoon, *J. Am. Chem. Soc.* **2007**, *129*, 1866–1867; b) D. J. Michaelis, M. A. Ischay, T. P. Yoon, *J. Am. Chem. Soc.* **2008**, *130*, 6610–6615; c) K. S. Williamson, T. P. Yoon, *J. Am. Chem. Soc.* **2010**, *132*, 4570–4571; d) K. S. Williamson; T. P. Yoon, *J. Am. Chem. Soc.* **2012**, *134*, 12370–12373.

Received: July 9, 2019

